cadherin Promoter in mice (Hennig, G., Löwrick, O., Birchmeier, W. & Behrens, J. Mechanisms identified in the transcriptional control of epithelial gene expression. J. Biol. Chem. 271, 595-602 (1996); Faraldo, M.L., Rodrigo, I., Behrens, J., Birchmeier, W & Cano, A. Analysis of the E-cadherin and P-cadherin promoters in murine keratinocyte cell lines from different stages of mouse skin carcinogenesis. Mol. Carcinog. 20, 33-47 (1997).

C1

Please delete the paragraph spanning page 7, line 28 through page 8, line 5, and replace it with the attached replacement paragraph:

C2

Analysis of the endogenous expression of Snail by RT-PCR in a panel of cell lines with varying E-cadherin expression demonstrated an inverse correlation between the expression of both molecules and a relationship between the expression of Snail an their invasive and metastatic capacity (Fig. 5). E-cadherin was observed in the epithelial, non-tumoral MCA3D cell line an in the PDV tumoral cell line, which in spite of its tumoral origin showed no invasive or metastatic capacity. However, the presence of Snail was not found in any of the cell lines. In contrast, in the tumour cell lines with invasive and metastatic capacity, HaCa4 and CarB, the absence of E-cadherin is associated with the presence of Snail.

Please delete the paragraph spanning page 10, line 20 through page 12, line 2, and replace it with the attached replacement paragraph:

The oligonucleotide which contains the sequence of the E-pal element of the mouse E-cadherin promoter (CD-E) (nucleotides -90 to -70) containing targets for the restriction enzymes SalI in 5' and XhoI in 3' was ligated in direct sense for a total of 6 complete repetitions using conventional techniques, isolation in polyacrylamide gels and cloning in pHISi vector (Clontech, Palo Alt, Ca) which contains the reporter gene HIS3 of *S. cerevisia* and replication elements of yeast, bacteria and appropriate selection genes. In this way, the expression of the HIS3 gene remains under the control of the multimerised E-pal element. Correct insertion of the regulatory sequences was verified by PCR, digestion with appropriate restriction enzymes and sequentiation. The bait vector thus generated was denominated pHIS-E6. The same method was used to generate vectors into which a mutant version of the E-pal element was introduced, also ligated 6 times in direct sense, in which the two central oligonucleotides, GC, were replaced by TT. The mutant bait vector generated was denominated pHIS-mE6. The bait vectors pHIS-E6 and pHIS-mE6 were independently integrated in the chromosomal locus URA3 of the yeast strain YM4271 (Clontech, Palo Alto, Ca) by the usual techniques for transformation and selection of stable strains which maintain growth in the presence of 20 mM 3-

aminotriazole (3AZT). The strains selected were denominated E-pal HIS3 (native E-pal construct) and mE-pal HIS3 (mutated E-pal construct). The yeast strain E-pal HIS3 was subjected to transformation with a commercial gene library of cDNA fron NIH3T3 cells which contains different inserts of cDNA fused to the GAL4 activation domain in the pACT2 vector (Clontec Palo Alto, Ca), previously amplified to obtain a titre of $3x10^6$ independent clones using conventional techniques. Transformant yeasts were selected for their ability to grow in the absence of Histidine and in the presence of 20 mM 3ATZ, and 300 independent clones were isolated. The plasmids containing the different sequences of cDNA were isolated from the transformant yeasts and were later used to transform *E. coli* (DH5a strain), recovering 221 independent *E. coli* clones, from which the corresponding plasmids were isolated. To eliminate false positives, the 221 plasmids were independently introduced in parallel into the previously generated yeast strains containing the HIS3 gene under the control of the wild E-pal element (E-pal HIS3 strain) or mutated E-pal (mE-pal HIS3 strain), selecting those plasmids which conferred growth in the absence of histidine and leucine and in the presence of 20 mM 3ATZ exclusively in the strain E-pal His3; the total number selected was 130. Inserts of these plasmids were initially analyse using digestion with various restriction enzymes and sequenced in an automatic sequencer. The sequences obtained were analysed in cDNA databanks using the BLAST/FASTA programme. 49% of the clones identified encoded the total or